

REVISED VERSION

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
5 August 2004 (05.08.2004)

PCT

(10) International Publication Number
WO 2004/064815 A1

(51) International Patent Classification⁷: **A61K 9/24**, 45/06

(21) International Application Number:
PCT/CA2004/000073

(22) International Filing Date: 21 January 2004 (21.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/441,156 21 January 2003 (21.01.2003) US

(71) Applicant (for all designated States except US): **SMART-
TRIX TECHNOLOGIES INC.** [CA/CA]; 16751 Tran-
sCanada Road, Kirkland, Quebec H9H 4J4 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ZERBE, Horst, G.**
[CA/CA]; 714 Main Road, Hudson, Quebec J0P 1H0 (CA).
SZABO, Pompilia [CA/CA]; 461 Boyd Avenue, Green-
field Park, Quebec J4V 1S4 (CA).

(74) Agents: **DUBUC, J. et al.**; Goudreau Gage Dubuc, Stock
Exchange Tower, 800 Place Victoria, Suite 3400, P.O. Box
242, Montreal, Quebec H4Z 1E9 (CA).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

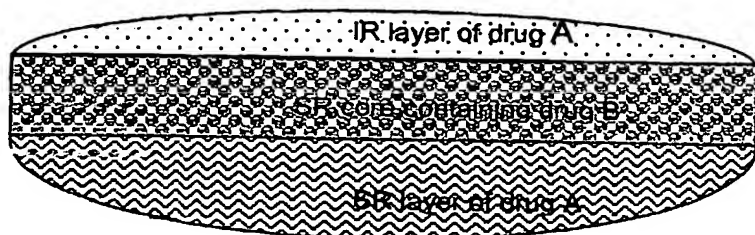
— with international search report

(88) Date of publication of the revised international search
report: 30 September 2004

(15) Information about Correction:
see PCT Gazette No. 40/2004 of 30 September 2004, Sec-
tion II

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: ORAL DOSAGE FORMULATION



(57) Abstract: A multi-layer oral dosage form, preferably a tablet, comprising a matrix core comprising a therapeutically effective amount of a first drug (NSAID), wherein the matrix core allows sustained release of the first drug; a first layer, which is in contact with the matrix core, comprising a first portion of a pharmaceutically effective amount of a second drug (H₂-blocker antagonist), wherein the first layer allows

sustained release of the second drug; and a second layer, which is in contact with said matrix core, comprising a second portion of the second drug, wherein the second layer allows immediate release of the second drug. Methods for preparing the multi-layer dosage form are also disclosed.

WO 2004/064815 A1

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA2004/000073

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/24 A61K45/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/098352 A (POZEN INC) 12 December 2002 (2002-12-12) page 3, line 30 - page 6, line 13 examples claims page 11, line 16 - line 21	1-64
A	WO 02/066002 A (GLAXO WELLCOME SA ; IBANEZ MATILDE FERNANDEZ (ES); SANZ EMILIO GARRIZ) 29 August 2002 (2002-08-29) page 2, line 1 - line 20 examples claims	1-64
A	US 4 946 685 A (EDGREN DAVID E ET AL) 7 August 1990 (1990-08-07) claims 5,6; figure 3; examples 28,30	1-64

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

27 May 2004

Date of mailing of the international search report

02.07.04

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3018

Authorized officer

Epskamp, S

INTERNATIONAL SEARCH REPORT

nation on patent family members

International Application No

PCT/CA2004/000073

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02098352	A	12-12-2002	CA 2449098 A1	12-12-2002
			EP 1411900 A2	28-04-2004
			WO 02098352 A2	12-12-2002
			US 2003069255 A1	10-04-2003
WO 02066002	A	29-08-2002	WO 02066002 A2	29-08-2002
			EP 1363604 A2	26-11-2003
US 4946685	A	07-08-1990	CA 1336070 C	27-06-1995
			US 4786503 A	22-11-1988
			AU 601033 B2	30-08-1990
			AU 1406588 A	06-10-1988
			BE 1001699 A3	13-02-1990
			CH 677447 A5	31-05-1991
			CA 1331739 C	30-08-1994
			DE 3811114 A1	10-11-1988
			ES 2006394 A6	16-04-1989
			FR 2613224 A1	07-10-1988
			GB 2203338 A ,B	19-10-1988
			GR 88100214 A ,B	31-01-1989
			IT 1219750 B	24-05-1990
			JP 2916147 B2	05-07-1999
			JP 63258808 A	26-10-1988
			KR 9503918 B1	20-04-1995
			LU 87189 A1	17-11-1988
			NL 8800867 A	01-11-1988
			SE 503611 C2	15-07-1996
			SE 8801240 A	07-10-1988
			ZA 8802034 A	15-09-1988

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/000073

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 28 and 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA2004/000073

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/24 A61K45/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/098352 A (POZEN INC) 12 December 2002 (2002-12-12) page 3, line 30 - page 6, line 13 examples claims page 11, line 16 - line 21	1-64
A	WO 02/066002 A (GLAXO WELLCOME SA ; IBANEZ MATILDE FERNANDEZ (ES); SANZ EMILIO GARRIZ) 29 August 2002 (2002-08-29) page 2, line 1 - line 20 examples claims	1-64
A	US 4 946 685 A (EDGREN DAVID E ET AL) 7 August 1990 (1990-08-07) claims 5,6; figure 3; examples 28,30	1-64

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

27 May 2004

Date of mailing of the international search report

07/06/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Epskamp, S

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA2004/000073

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02098352	A	12-12-2002	CA 2449098 A1	12-12-2002
			EP 1411900 A2	28-04-2004
			WO 02098352 A2	12-12-2002
			US 2003069255 A1	10-04-2003
WO 02066002	A	29-08-2002	WO 02066002 A2	29-08-2002
			EP 1363604 A2	26-11-2003
US 4946685	A	07-08-1990	CA 1336070 C	27-06-1995
			US 4786503 A	22-11-1988
			AU 601033 B2	30-08-1990
			AU 1406588 A	06-10-1988
			BE 1001699 A3	13-02-1990
			CH 677447 A5	31-05-1991
			CA 1331739 C	30-08-1994
			DE 3811114 A1	10-11-1988
			ES 2006394 A6	16-04-1989
			FR 2613224 A1	07-10-1988
			GB 2203338 A ,B	19-10-1988
			GR 88100214 A ,B	31-01-1989
			IT 1219750 B	24-05-1990
			JP 2916147 B2	05-07-1999
			JP 63258808 A	26-10-1988
			KR 9503918 B1	20-04-1995
			LU 87189 A1	17-11-1988
			NL 8800867 A	01-11-1988
			SE 503611 C2	15-07-1996
			SE 8801240 A	07-10-1988
			ZA 8802034 A	15-09-1988